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## RIFAMPICIN SERUM LEVEL IN EGYPTIAN TUBERCULOUS PATIENTS

By

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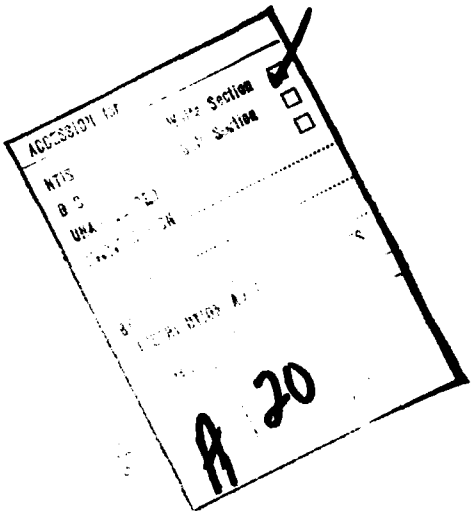
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# *Rifampicin Serum Level in Egyptian Tuberculous Patients**

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M. E. Mahmoud,+ A. El Maraghi,+ and Adly Robert +

## ABSTRACT

**This report includes the microbiological determination of Rifampicin (RMP) serum levels in 26 chronic tuberculous Egyptian patients who received the drug for the first time. RMP mean serum levels at 3 and 6 hours after its oral administration in therapeutic doses ( 450/600 mg daily ), were 5.01 μg/ml ( S.D. ± 3.14 ) and 3.53 μg/ml ( S.D. ± 1.3 ) respectively. RMP serum levels at 3 and 6 hour samples exceeded 0.2 μg/ml in all patients.**

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## Introduction

Several investigators have demonstrated the therapeutic efficacy and minimal drug toxicity of Rifampicin (RMP). Gyselen et al. (1968; 1969) reported that RMP produces substantial antimycobacterial effects in pulmonary tuberculosis. Pickroth et al. (1969) reported that there are no side effects with RMP. Constans and associates (1968) correlated the serum level of RMP with the functional condition of the gastrointestinal tract and its entero-hepatic cycle, while Meola (1968), correlated serum levels and RMP dose to body weight. The trend of RMP serum levels after oral administration in Egyptian tuberculous patients is reported in this study.

## Material and Methods

**Subjects :** Twenty-six patients ( one female and 25 males ) between the age of 25 and 50 years were included in this study. All of them were suffering from chronic pulmonary tuberculosis and were treatment failures to Streptomycin, PAS and INH.

**Treatment Schedule :** Rifampicin was administrated in a dose of 450/600 mg depending on the body weight. Those below 60 kg received 450 mg. Rifampicin was given before breakfast since the drug is more efficiently absorbed in a patient with an acid pH (Hussels, 1969). None of the patients received RMP before the trial. The duration of treatment with the drug before collection of the blood samples in most of our patients did not exceed one week, thereby preventing drug serum level variation due to prolonged treatment. In order to determine if prolonged treatment with RMP affects drug levels, RMP assays were repeated in 3 patients ( cases 24, 25 and 26) after they had received the drug for one month.

**Specimens :** Five milliliter blood samples were taken from each patient at 3, 6 and 24 hours after initiation of therapy.

**Drug Assay :** Rifampicin concentrations in the sera were bioassayed by the agar — diffusion method employing simultaneous parallel comparison with standards, using **Sarcina**

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**lutea** ( ATCC 9341) as the test organism. One ml. of an optical density 0.35 at 550 mu test organism suspension was added to 300 ml. Sensitivity Test Medium ( Oxoid). A Rifampicin stock solution of 1000 $\mu$g/ml was prepared in dimethyl-formamide and stored in -70°C. From this stock a working standard solution of a concentration 0.25 ; 0.5 ; 1 ; 2 ; 4 ; 8 and 16 $\mu$g/ml was prepared in a pooled, pretested normal human serum. Each assay involved three replications of the test serum and RMP standards using sterile filter paper discs ( ¼" ). Results were analyzed by ( method 2) recommended by Bennett et al. (1966).

## Results

Rifampicin levels obtained after a single dose in 26 pulmonary tuberculosis Egyptian patients at 3, 6 and 24 hours are represented in Table 1. The mean serum levels were 5.01 $\mu$g/ml ( S.D. $\pm$ 3.14 ) at 3 hours and 3.53 $\mu$g/ml. ( S.D. $\pm$ 1.3 ) at 6 hours. After 24 hours RMP concentration was nil in 25 patients and 0.2 $\mu$g/ml in case 13 (Table 1).

Serum levels in the 3 patients repeated after prolonged treatment with RMP for one month are shown in Table 2. Case 24 had higher serum RMP levels than those reported at the beginning of treatment ( i.e. 9.9 $\mu$g/ml versus 7.3 $\mu$g/ml at 3 hours ) with accumulation of the drug after 24 hours ( 0.65 $\mu$g/ml versus nil ). Cases 25 and 26 showed lower RMP serum levels at 3 hours after prolonged treatment.

## Discussion

The levels of Rifampicin in blood obtained in 26 Egyptian tuberculous patients compared very well with the RMP concentrations in blood obtained by Verbist (1969) at the 3 and 6 hour samples. Although there was a large difference in peaks between the individuals at 3 hour samples, 50% of them (13/26) reached peak values greater than 5 $\mu$g/ml (Table 1). Still, 6 hour RMP serum levels of all patients were above the minimal inhibitory concentration of tubercle bacilli which was determined by Dickinson and Mitchison 1970 (0.2 $\mu$g).

Previous studies ( Dettli et al., 1968 ; and Verbist, 1969 ), found that RMP blood levels of patients treated with the drug for several weeks were lower than those attained during the first week of treatment. We found that one of the three patients with a prolonged treatment showed an exception to this trend. His RMP serum levels at 3 and 6 hours were higher than those reported at the beginning of the treatment. Also, 2 of these patients showed a remarkable accumulation of the drug after 24 hours (Table 2).

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TABLE 1.

Rifampicin Serum Concentrations in Tuberculous Patients

| Patients | $\mu_g$ Rifampicin per ml of Serum | | |
|---|---|---|---|
| | Hours after dosage | | |
| | 3 | 6 | 24 |
| 1. A.A.A. | 3.50 | 3.10 | 0.00 |
| 2. G.H.G. | 10.40 | 5.60 | 0.00 |
| 3. H.I. | 0.28 | 5.40 | 0.00 |
| 4. A.A.E.S. | 2.85 | 1.20 | 0.00 |
| 5. A.E.M.T. | 3.70 | 1.60 | 0.00 |
| 6. G.Z. | 0.34 | 5.70 | 0.00 |
| 7. A.M.I. | 8.40 | 4.70 | 0.00 |
| 8. M.S. | 3.35 | 3.65 | 0.00 |
| 9. S.A. | 0.28 | 1.15 | 0.00 |
| 10. M.E.B. | 4.10 | 2.25 | 0.00 |
| 11. G.S. | 4.95 | 3.30 | 0.00 |
| 12. S.H.E.S. | 6.85 | 4.70 | 0.00 |
| 13. H.M.E.S. | 6.75 | 5.40 | 0.20 |
| 14. M.M. | 11.00 | 5.80 | 0.00 |
| 15. S.M. | 7.10 | 2.70 | 0.00 |
| 16. A.I.A. | 4.70 | 2.10 | 0.00 |
| 17. A.G.A.G. | 7.70 | 3.80 | 0.00 |
| 18. Y.N. | 5.30 | 2.40 | 0.00 |
| 19. H.M.S. | 3.00 | 1.10 | 0.00 |
| 20. K.A.E.S. | 3.20 | 3.40 | 0.00 |
| 21. B.G. | 0.26 | 5.00 | 0.00 |
| 22. H.R. | 6.40 | 3.80 | 0.00 |
| 23. A.M. | 0.47 | 3.00 | 0.00 |
| 24. S.M. | 7.30 | 4.30 | 0.00 |
| 25. F.A. | 8.20 | 3.10 | 0.00 |
| 26. E.A. | 7.80 | 3.70 | 0.00 |
| Mean | 5.01 | 3.53 | 0.007 |
| S.D. $\pm$ | 3.14 | 1.30 | — |

TABLE 2.

Rifampicin Serum Concentrations after Prolong treatment (Patients 24, 25 and 26)

| Patients | $\mu_g$ Rifampicin per ml of Serum | | |
|---|---|---|---|
| | Hours after dosage | | |
| | 3 | 6 | 24 |
| 24. S.M. | 9.90 | 5.70 | 0.65 |
| 25. F.A. | 4.80 | 1.60 | 1.03 |
| 26. E.A. | 6.00 | 1.40 | 0.00 |

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